

# PHANTOM LIMB PAIN IMPROVEMENT POST RIGHT LOWER EXTREMITY AMPUTATION WITH A LINER-TYPE PROSTHESIS AND PHARMACOTHERAPY COMBINATION: A CASE REPORT

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**Background:** Phantom limb pain is pain in a missing limb postamputation. There is no sufficient evidence for an effective drug therapy, even though various treatment methods have been tried. Apart from drug therapy, mirror therapy, proprioceptive training, and virtual reality, as well as rehabilitation with appropriate orthotics have been tried. Liner-type prostheses use a silicone liner to reduce shear forces between the skin and the orthosis and to maintain suspension function, thereby relieving pain and improving comfort and functionality for the user.

**Case Report:** A 65-year-old man underwent amputation of his right thigh. On the 10th postoperative day, he complained of phantom limb pain centered on the amputation site. Pregabalin was started but did not alleviate his symptoms. After consultation with a physical therapist, the patient began using a liner prosthesis on the 33rd postoperative day. Symptoms gradually lessened, and positive comments were heard from the patient. Pregabalin and duloxetine were administered for a time but were soon reduced. Due to good pain control, the patient was discharged on the 46th postoperative day. After discharge from the hospital, the patient was able to continue treatment as an outpatient without his symptoms worsening, using a liner prosthesis as needed.

**Conclusion:** Right thigh amputation is a very physically and emotionally taxing operation for the patient. Phantom limb pain is a difficult symptom to manage, but it must be adequately controlled for the patient. We have achieved phantom limb pain improvement with a combination of pharmacotherapy and a liner prosthesis. We feel a great need for close collaboration with other professions and for a nonpharmacologic approach in addition to pharmacotherapy.

**Key words:** Phantom limb pain, amputation, pregabalin, duloxetine, liner type prosthesis

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## BACKGROUND

Phantom limb pain (PLP) is a symptom that occurs in 60%–80% of patients with a missing limb. PLP is when a patient feels pain as if the missing limb were present. The causal mechanism is complex and has multiple factors; the peripheral nerves, the spinal cord, and brain are thought to be involved (1). Various drug therapies have been tried to date, but an optimal treatment has not been established (2). In addition to drug therapy, electrical stimulation, rehabilitation with appropriate orthotics, and behavioral cognitive therapy have been tried (3). A liner-type prosthesis uses a silicone liner to reduce the shear force between the skin and the socket, thereby eliminating the cause of pain and abrasions. In addition, the suspension function is securely maintained, providing increased comfort and functionality for the user (4).

We report a case of PLP post amputation of the right thigh, which was treated with a combination of a liner prosthesis along with pregabalin and duloxetine.

## CASE PRESENTATION

A 65-year-old man underwent amputation of the right thigh for a refractory ulcer at the site of angiosarcoma removal. On the 10th postoperative day, the patient complained of PLP, saying “I feel pain at the site of the original wound” and “I feel pain, but does it really hurt?”

He was being treated for lymphedema of the lower extremities. He was referred to our hospital for close examination and treatment because a lump appeared on his right lower leg without any trigger; the lump gradually increased in size. A biopsy revealed angiosarcoma, and the patient underwent subcutaneous tumor resection of the right lower extremity. An ulcer developed due to postoperative infection of the site, resulting in a foul odor, severe exudate, and exposed bone. Daily treatment was difficult, and the odor made it difficult to invite friends to his house, resulting in a marked decline in quality of life. The patient decided to have his right thigh amputated, and surgery was performed.

The patient's additional medical history included varicose veins in the right lower extremity, diabetes mellitus, and hypertension. His family history of cancer included maternal pancreatic cancer. No specific medications or allergies were noted. Upon physical examination at the time of the phantom pain's appearance, the patient had a height of 174.1 cm, a body weight of 70.4 kg, a pulse

of 89 beats/min, a blood pressure of 144/84 mm Hg, and a body temperature of 37°C. Edema of the right lower extremity was prominent. Laboratory tests at PLP's onset showed that the patient was slightly anemic, with low albumin and cholinesterase. Fasting blood glucose was slightly elevated (Table 1).

He had been taking oxycodone hydrochloride hydrate tablets preoperatively at a dose of 80 mg/d. Continuous oxycodone hydrochloride hydrate injection at 96 mg/d was started after intravenous patient-controlled analgesia (iv PCA: fentanyl citrate injection 756 µg/d) for postoperative pain. Wound pain tended to lessen and oxycodone hydrochloride hydrate was reduced (Fig.1).

However, on the 10th postoperative day, the patient reported PLP. Pregabalin was started at 50 mg/d and gradually increased to 300 mg/d. Oxycodone hydrochloride hydrate for wound pain was gradually decreased and discontinued (Fig.2), but his phantom pain did not improve. The patient continued to report that “there is no pain when I press down on the cut area, but I feel pain where my foot originally was.” After consulting with a physical therapist, introducing a liner-type thigh prosthesis was considered, it was started on the 33rd postoperative day.

The patient's comments were positive, such as, “Wearing the orthotic made me feel more comfortable because my leg felt protected.” As the patient became accustomed to using the prosthesis, the pain became closer to the “real pain point” and the PLP improved.

Pregabalin was temporarily increased to 375 mg/d, but was gradually decreased to 150 mg/d due to a lack of efficacy and increased drowsiness. Duloxetine was started at 20 mg/d and there was no worsening of pain. The duloxetine dose was subsequently increased to 40 mg/d. The patient commented that “The pain is getting better,” so the phantom pain was being well controlled. Our patient was discharged on the 46th postoperative day (Fig.3).

After discharge, the patient used the prosthesis only when necessary and was able to make self-decisions. All analgesic adjunctive medications were terminated, but no worsening of pain was observed. He reported, “I am in good condition after leaving the hospital” and “I am glad I had the lower limb amputated.” His wife said, “As a caregiver, I feel much better.” The couple was able to go about their daily lives without inconvenience and maintain their quality of life.

Although 18F-fluorodeoxyglucose-positron emission tomography on the 75th postoperative day revealed

Table 1. The laboratory data at onset of phantom limb pain.

White Blood Cell count	5.7	103/ $\mu$ L	Total protein	5.1	g/dL
Hemoglobin	9.8	g/dL	Albumin	2.9	g/dL
Platelet	230	103/ $\mu$ L	Cholinesterase	168	U/L
CRP	0.25	mg/dL	Total Bilirubin	0.2	mg/dL
Sodium	138	mmol/L	AST	15	U/L
Potassium	4.4	mmol/L	ALT	16	U/L
Chlorine	105	mmol/L	CK	22	U/L
Calcium	9.0	mg/dL	ALP	57	U/L
BUN	26	mg/dL	$\gamma$ -GT	12	U/L
Creatinine	0.76	mg/dL	Blood sugar	143	mg/dL

CRP: C-creative protein, BUN: blood urea nitrogen, AST: aspartate aminotransferase

ALT: alanine aminotransferase, CK: creatine kinase, ALP: alkali phosphatase

$\gamma$ -GT:  $\gamma$ -glutamyltransferase

multiple lung metastases in both lungs, the patient did not exhibit any depression and remained motivated to continue chemotherapy treatment for recurrent lung metastases, saying, "I decided to try a new treatment."

## DISCUSSION

PLP is a constant or intermittent unpleasant sensation or pain in the area of the amputated limb, as if a lost limb were present. It is estimated to occur in 60%–80% of patients with amputated limbs (1). Pain persists for long periods of time and reduces quality of life (5). However, the frequency and duration of PLP usually decrease within the first 6 months postamputation (6-9). Our patient's symptoms almost disappeared at approximately 3 months, which is consistent with these studies. PLP's pathogenesis is thought to involve functional changes in the sensorimotor cortex and functional restructuring at the level of the higher central nervous system, such as the spinal cord, due to the loss of signal input from the missing limb, but this is still unclear (10,11).

As for drug therapy, the guidelines of the Japan Pain Clinic Society recommend  $\text{Ca}_2^+$  channel  $\alpha_2\delta$  ligands (e.g., pregabalin, gabapentin), serotonin/noradrenaline re-uptake inhibitors (e.g., duloxetine), or tricyclic antidepressants (e.g., amitriptyline, nortriptyline, imipramine) as first-line drugs. Tramadol and vaccinia virus-inoculated rabbit inflammatory skin extract are recommended as second-line agents, and opioid analgesics are recommended as third-line agents (12). While pharmacologic treatment for PLP has been explored,

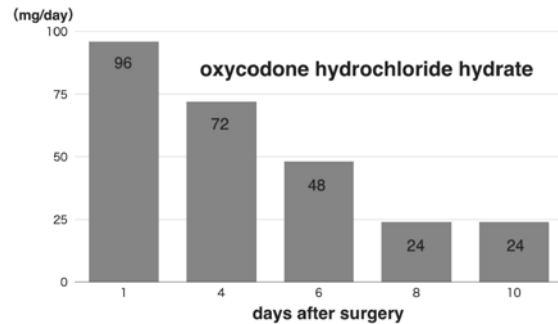


Fig. 1. Wound pain tended to decrease. Postoperatively started oxycodone hydrochloride hydrate injections were able to be tapered off.

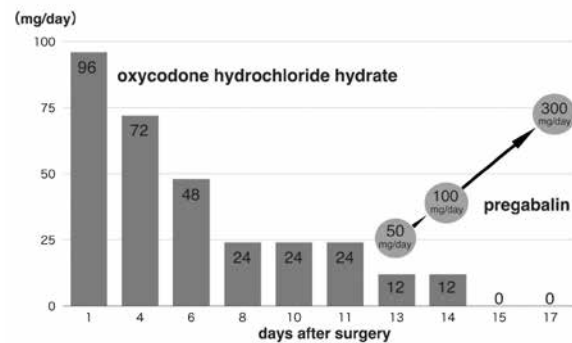


Fig. 2. Pregabalin was started at 50 mg/d on the 13th postoperative day and titrated up, depending on the intensity of symptoms. Oxycodone hydrochloride hydrate injection for wound pain was gradually decreased and discontinued on the 15th postoperative day.

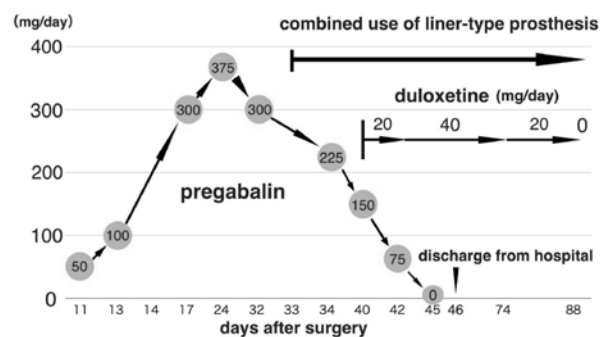


Fig. 3. Increasing the dose of pregabalin alone did not improve the phantom pain. A liner prosthesis was started on the 33rd postoperative day and duloxetine was started on the 40th postoperative day. The phantom pain improved and pregabalin was tapered off on the 45th postoperative day. The patient was discharged on the 46th postoperative day.

several reviews have not found convincing evidence for its efficacy. A recent Cochrane analysis of 14 studies with 269 patients only found limited evidence for pharmacotherapy (2). Despite this, gabapentinoids or antidepressants may be used for the 10% of amputees who experience severe PLP after 6 months or longer.

As for nonpharmacologic therapies, effective methods include mirror therapy, proprioceptive training, virtual reality, or an advanced prosthetic (13-16). Studies show that prosthetic usage can reduce PLP by restoring sensory feedback, reducing sensorimotor incongruence, and improving body awareness (17-19). Prostheses remain the best documented treatment for PLP (20,21).

Liner-type prostheses are used by attaching a silicone liner between the socket and the amputated leg. It acts as a buffer between the socket and the skin, reducing shearing forces on the skin of the amputated leg and ensuring that the prosthesis has a suspension function (4). The use of assistive devices may not be suitable for all cases because of the financial burden involved but should be considered as a nonpharmacologic treatment.

Our patient improved when we prescribed pregabalin and duloxetine as pharmacologic therapy and a liner prosthesis as nonpharmacologic therapy; he did not proceed with treatment by medication alone. After consulting with other professionals, a combined use of orthotics was attempted, which led to a reduction in symptoms. Postoperative orthosis was introduced at a relatively early stage, allowing rehabilitation to

proceed smoothly. This kept the patient motivated to continue treatment. He had just undergone a physically and emotionally demanding operation to amputate his lower limb. It was essential to improve his phantom pain so that he would not regret his treatment.

Our patient decided to have his right thigh amputated due to significant preoperative deterioration of his quality of life. PLP was a postamputation symptom of his right lower extremity. Improving his PLP symptoms was essential to avoid his regretting the decision to amputate. Treatment does not always proceed smoothly and can be difficult (22). That is why we needed to consult with other professions (in this case, physicians, nurses, pharmacists, and physical therapists) to find the best treatment. The combined use of a liner-type prosthesis and pharmacotherapy contributed greatly to the symptom improvement in this case. This case makes us keenly aware once again of the need to consider treatment methods from various occupational fields.

## CONCLUSION

Amputation at the thigh is a physically and emotionally taxing treatment.

PLP is a difficult symptom to manage, but in this case, the using a liner prosthesis was effective. In collaboration with other professions, it is necessary to provide not only pharmacologic therapy but also nonpharmacologic therapy in parallel.

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